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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/091,281	03/06/2002	Vincent Raymond	13587.338	7473

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EXAMINER	
TUNG, JOYCE	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 03/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No. 10/091,281	Applicant(s) RAYMOND ET AL.	
	Examiner Joyce Tung	Art Unit 1637	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 11 March 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 2 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The reply was filed after the date of filing a Notice of Appeal, but prior to the date of filing an appeal brief. The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *22, 25-32, 35-36, 40, 52-56*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: please see the attached.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

The applicant's response filed 2/28/05 the Office action has been entered. Claims 22, 25-32, 35-36, 40, 52-56 are pending.

1. The rejection of Claims 22-40 under 35 U.S.C. 112, second paragraph is withdrawn because of the argument.

2. Claims 22-23, 25-33, 35-38, 40, and 56 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number'' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

All of the current claims encompass a genus of nucleic acids, which is a polymorphism in a promoter region of the optineurin gene, which are not disclosed in the specification. The genus includes an enormous number of polymorphisms for which no written description is provided in the specification. This large genus is represented in the specification by only the polymorphisms listed in Table 1 (See pg. 18 of the specification) for which data is provided demonstrating an association with the identification of risk for developing glaucoma or a progression from an

ocular hypertensive state and may be associated with therapeutic responsiveness (see pg. 17). Thus, applicant has express possession of only particular polymorphisms listed in Table 1, in a genus, which comprises hundreds of millions of different possibilities. Here, no common element or attributes of the sequences are disclosed which would permit selection of sequences as polymorphisms. No structural limitations or requirements which provide guidance on the identification of sequences which meet the functional limitations of associating a polymorphism for diagnosing glaucoma by detecting a polymorphism in a promoter region of the optineurin gene is provided. Further, these claims expressly encompass all the different possible allelic variants including insertions, deletion, substitutions and transversions at thousands of different sites. No written description of alleles, of upstream or downstream regions containing additional sequence, which are associated with the polymorphism in a promoter region of the optineurin gene.

The response argues that in combination with the complete nucleotide sequence of SEQ ID NO: 1, the single nucleotide polymorphisms listed in Table 1 reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention. However, the single nucleotide polymorphisms listed in Table 1 has 18 single polymorphisms, which are not listed in the claims 22, 32, and 36. In addition, there is no description that how the marker nucleic acid molecules are used to detect each single polymorphism in table 1. Thus the rejection is maintained.

3. Claims 22-23, 25-33, 35-38, 40 and 56 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the marker which is capable of detecting a SNP set forth in Table 2, does not reasonably provide enablement for using any

marker nucleic acid molecule having a nucleic acid sequence that specifically hybridizes to a sequence selected from the group consisting of SEQ ID NO: 1 and complement thereof, and a complementary nucleic acid molecule obtained from a sample. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404.

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The claims are drawn to a method for diagnosing glaucoma in a sample obtained from a cell or a body fluid by detecting a polymorphism in a promoter region of the optineurin gene comprising using a marker nucleic acid molecule having a nucleic acid sequence that specifically hybridizes to a sequence selected from the group consisting of SEQ ID NO: 1 and a complement thereof, and a complementary nucleic acid molecule obtained from a sample under nucleic acid hybridization condition, permitting the hybridization and detecting the presence of the polymorphism. The invention is in a class of invention, which has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The breadth of the claims

The claims encompass any nucleic acid selected from the group consisting of the 5054 nucleotides of SEQ ID NO: 1 which will be used as a marker nucleic acid. Thus, the claims claim 5054 different nucleic acids markers. These species even have less utility in the very large genus for diagnosing glaucoma via detecting a polymorphism in a promoter region of the optineurin gene.

Quantity of Experimentation

The quantity of experimentation in this area is extremely large since determination of a use for the many sequences would require, initially, studies to demonstrate some utility or use. This study is an inventive, unpredictable and difficult undertaking in itself, and utility would need to be demonstrated by some association such as an epidemiological study. This would require years of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

The unpredictability of the art and the state of the prior art

The art in biotechnology, as relates to the association of diseases with particular genes, is highly unpredictable. For example, In Rezaie et al (Science, 2002, Vol. 295(8)), Rezaie et al. indicate that the identification of *OPTN* as an adult-onset glaucoma gene provides an opportunity to screen the general population because *OPTN* mutations are a contributing factor in patients with normal pressure glaucoma (NPG) (See pg. 1079, column 2, last paragraph). However, Rezaie et al. do not disclose a nucleic acid marker having a nucleic acid sequence that specifically hybridizes to a sequence selected from the group consisting of SEQ ID NO: 1 and a complement thereof, and a complementary nucleic acid molecule obtained from a sample.

Working Examples

The specification has a working example of the identification of SNPs in the optineurin promoter. The method applies genomic DNA from 23 individuals sequenced (See pg. 111-113). Nevertheless, the method does not apply the marker nucleic acid molecule having a nucleic acid sequence that specifically hybridizes to a sequence selected from the group consisting of SEQ ID NO: 1 and a complement thereof and a complementary nucleic acid molecule obtained from a sample.

Guidance in the Specification.

The specification provides no guidance on uses for the marker nucleic acid.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

In the instant case, as discussed above, the level of unpredictability in the art is high (see Rezaie et al.), the specification provides one with no written description or guidance that leads one to a reliable method of using the marker nucleic acids for diagnosing glaucoma in a sample obtained from a cell by detecting a polymorphism in a promoter region of the optineurin gene One of skill in the art cannot readily anticipate the effect of a change within the subject matter to which the claimed invention pertains. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of any working examples and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

The response argues that the specification provides ample guidance to teach to worker of ordinary skill how to make and use the claimed invention without undue experimentation. The response lists the page numbers of the guidance. However there are still no enough examples to describe using each marker nucleic acid molecule from the group consisting of SEQ ID NO: 1 for diagnosing glaucoma in a sample. Thus the rejection is maintained.

4. The claims 52-55 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the marker which is capable of detecting a SNP at location 709 as set forth in Table 4, does not reasonably provide enablement for using any polymorphisms of SEQ ID NO: 1 and a complementary nucleic acid molecule obtained from a sample as cited in claims 52 and 54 for diagnosing glaucoma via detecting the single nucleotide polymorphism of SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The response does not address the argument concerning claims 52-55. Thus, the rejection is maintained.

Summary

5. No claims are allowable.

6. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (571) 272-0790. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (571) 272-0782 on Monday-Friday from 10:00 AM-6:00 PM.

7. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1637 via the PTO Fax Center located in Crystal Mall 1 using (571) 272-8300.

Joyce Tung
J. Tung
March 15, 2005

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
3/16/05